APPENDIX D

International Preliminary Examination Report

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
2003946-0018		
International application No. PCT/US 03/07377	International filing date *(day/month/year)* 07.03.2003	Priority date *(day/month/year)* 08.03.2002
International Patent Classification (IPC) or both national classification and IPC C07D313/00		
Applicant EISAI CO. LTD. et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 9 sheets, including this cover sheet.

   ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 44 sheets.

3. This report contains indications relating to the following items:

   I ☒ Basis of the opinion
   II ☐ Priority
   III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   IV ☐ Lack of unity of invention
   V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   VI ☐ Certain documents cited
   VII ☐ Certain defects in the international application
   VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
25.09.2003	29.06.2004
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer Kirsch, C Telephone No. +49 89 2399-2191

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/US 03/07377

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:

Description, Pages

1-377 as originally filed

Claims, Numbers

12-19, 53-58, 59 (part), 97-105 as originally filed

1-11, 20-52, 59 (part), 60-96, 106-126 received on 30.04.2004 with letter of 28.04.2004

Drawings, Sheets

1/9-9/9 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

5. ☒ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

   see separate sheet

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

   ☐ the entire international application,

   ☒ claims Nos. 84-126

   because:

   ☒ the said international application, or the said claims Nos. 84-126 relate to the following subject matter which does not require an international preliminary examination (specify):

   see separate sheet

   ☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

   ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

   ☐ no international search report has been established for the said claims Nos.

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

   ☐ the written form has not been furnished or does not comply with the Standard.

   ☐ the computer readable form has not been furnished or does not comply with the Standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	22-36,66-80,108-118
	No:	Claims	1-21,37-65, 81-107,119-126
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-126
Industrial applicability (IA)	Yes:	Claims	1-83
	No:	Claims	

2. Citations and explanations

see separate sheet

Reference is made to the following documents:

D1: EP-A-0 606 044
D2: WO96/13259
D3: WO00/38674
D4: Agastuma T. et al., Chem. Pharm. Bull., 1993, 41(2), 373-375
D5: Takehana K. et al., Biochem. Biophys. Res. Comm., 199, 257, 19-23
D6: WO02/48136 (P-document)

Document D6 published 20.06.2002 with filing date of 13.12.2001 and claiming priority date of 14.12.2000 has been found in a search of the state of the art in accordance with Art. 33(2) and (3) and rule 64.3 PCT. This document will not be taken into account in international phase, however, the attention of the applicant is drawn to the fact that it may prove relevant when assessing novelty and inventive step in the regional phases.

The present application deals with macrolactone analogs of zearalenone having (Z)-configuration at C-5-C-6 and (S)-configuration at C-8 and their use as antiinflammatory, immunosuppressive, anticancer and antiageing agents.

Re Item I
Basis of the report

Excluding protection for part of the subject-matter of the claimed invention, as covered by the application as filed, by disclaiming a certain anticipation in the state of the art is acceptable under the terms of Article 34(2)b PCT only if the following conditions are met:

(i) the subject-matter disclaimed must be precisely defined and strictly limited to the actual scope of the anticipation, and

(ii) said anticipation must be a so-called "chance anticipation", which means that it would be regarded as accidentally falling within the terms of the claim(s) of the application.

Condition (ii) specifically refers to cases where the anticipation is of a chance nature in that

what is disclosed in the prior document could accidentally fall within the wording of the claim(s) of the application to be assessed for novelty without there being a common or related technical field, or a common technical problem or solution. In other words, **the prior document must form part of an entirely remote and unrelated state of the art** which the skilled person, faced with the assessment of inventive step, would normally never take into consideration.

When carrying out the comparison in the present case it is found that the relevant disclosure in citations D1-D5 relates to macrolactone analogs of zearalenone and their use as antiinflammatory, or anticancer agents and, accordingly, to exactly the same technical field solving exactly the same technical problem as the claimed invention. Since the state of the art referred to in citations D1-D5 is highly relevant to the claimed subject-matter in the application, condition (ii) is clearly not met. Accordingly, the disclaimer is not allowable within the framework of Article 34(2)b PCT and, consequently, the amendment as a whole is not acceptable. Therefore, this report has been drafted as if no disclaimer has been introduced.

The expressions "pharmaceutically acceptable derivatives" and "lower alkyl" have been clarified in the light of the description. Support for these modifications can be found in paragraphs [0087] ans [0090] respectively. These amendments are in accordance with the requirements of Art. 34(2)b PCT.

Re Item III
Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

Claims 84-126 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

Re Item V
Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Document D1 describes macrolactone analogs of zearalenone useful as cytokine release inhibitors and IL-1 antagonists for the treatment of inflammatory disorders. Formula (I) of D1 overlaps with the definition given in the present application where a-b is a cis-C=C, C is C=O and d is (S)-CH(OR). Such structural features are disclosed in claims 2-4 and 6 and are illustrated in formula (I'), examples 8 and 10. Since no structural element common to all the possibilities comprised in this overlap could be identified, the present claimed subject-matter cannot be considered novel over D1 (Art. 33(2) PCT).

Document D2 discloses macrolactone analogs of zearalenone which inhibit protein kinases such as tyrosine kinases and can therefore be used in the treatment of various diseases including cancers and restenosis (see p. 12-14). On the basis of claim 1, it turns out that there is an overlap between the claimed subject-matter and the teaching of D2 when the configuration at positions 3, 5-6 and 8 in formula (I) of D2 are as described in the present application. These features are disclosed in claims 9 and 10 and on p. 9, l. 6-7 as well as in compound C292 which falls within the scope of the present invention.
Consequently, no new technical element common to the compounds of the present application which fall within the overlap and which can be regarded as adding a new element to the state of the art could be identified sofar. Since, this new technical feature, which is necessary to established novelty, fails, this overlap is considered identical to what has already been disclosed in D2 (Art. 33(2) PCT).
The content of D2 is neither limited to its examples nor to the preferred embodiments disclosed therein. The content of D2 should be regarded as a whole and all the information contained therein is state of the art in the sense of Art. 33(2) PCT.

Document D3 reveals zearalenone derivatives which affect mRNA stability and are useful in the treatment of cancer and inflammatory diseases. Formula (II) of D3 overlaps with formula (I) according to the present application when a-b is a cis-C=C, C is C=O and d is (S)-CH(OR). These structural features are described on p. 6, last 2 lines and in formula (III). Since no new technical element which could provide a contribution over the prior art could be identified, the subject-matter of the present application is considered to lack novelty (Art. 33(2) PCT). In order to established novelty, the applicant should identify a new structural element which is common to all the alternatives comprised in the overlap and which is not disclosed in the prior art.

Document D4 discloses the corrected structure hypothemycin which exhibit antiproliferative activity on P388 cell lines and the synthesis of analogs thereof. Hypothemycin (1) as well as its triacetate (3) fall within the scope of claim 1. Claim 1 lacks novelty with regard to document D4 (Art. 33(2) PCT).

Document D5 deals with the biological activity of radicicol related compounds and especially their mechanism of action on cancer cell lines. The compounds 87-250904-F1 and LL-Z1640-2 both fall within the scope of the present invention. The subject-matter of claim 1 is not novel with regard to the disclosure of D5 (Art. 33(2) PCT).

2. The only structural element common to all the compounds claimed is the presence of a zearalenone core structure with a cis double at C-5-C-6 and (S)-configuration at C-8 . Such a structural feature is already disclosed in documents D1 to D5 for compounds which exhibit the same biological activity. Since the common feature is not novel, it cannot represent the single inventive concept which could have linked the different claimed subject- matters together.

The technical relationship between the different subject-matters of claims 1-126 required by rule 13.1 PCT is missing and the requirement for unity of invention does not seem to be fulfilled.

3. Document D6 describes the use of zearalenone derivatives as keratinocytes proliferation inhibitors in the treatment or the prevention of skin diseases. The compounds of formula (1), (4), (8)-(9) and (11) differ from the present claimed subject-matter due to the absence of specific configurations for the chiral carbon atoms at positions 3 and 8. Novelty is acknowledged with regard to document D6 (Art. 33(2) PCT).

4. Documents D1 to D5, which are considered to represent the most relevant state of the art, disclose macrolactone analogs of zearalenone and their use in the treatment of various diseases such as cancer and inflammatory disorders.

The problem to be solved by the present application may be considered as the provision of zearalenone derivatives for use as pharmaceutical agents.

Since zearalenone derivatives and their use as anticancer and antiinflammatory agents is already known from D1 to D5, the subject-matter cannot be considered inventive with regard to the disclosure of the prior art documents (Art. 33(3) PCT). Having regard to the similar compounds of D1 to D5, the problem may be reformulated as consisting in the obtention of further zearalenone derivatives for use as pharmaceutical agents with unexpected properties. Since no comparative data which could illustrate the presence of such properties for the claimed compounds are available, the problem has not been solved and inventive step cannot be acknowledged (Art. 33(3) PCT).

5. For the assessment of the present claims 84-126 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

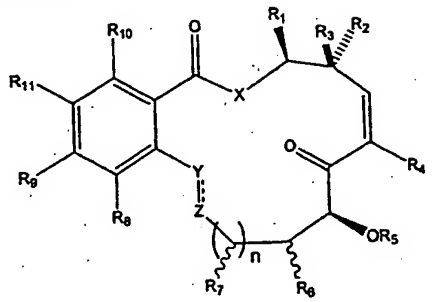
6. The breadth of the claims should be such that it represents a reasonable generalisation over the examples provided (cf. Guidelines C-III, 6.2 and C-II, 4.9), and especially such that every compound falling within its scope actually provides a solution to the problem underlying the invention.

In the present case, the definitions "(hetero)aliphatic", "(hetero)alicyclic", "(hetero)aryl", "protected hydroxyl or amino", "alkyloxy", etc. used in the claims without precision about the number of carbones or of heteroatomes, the size of the cycles or the kind of substituents, is vague and imprecise and could comprise compounds which would not exhibit the claimed activity (Art. 33(3) PCT).

CLAIMS

We claim:

1. A compound having the structure:



(I)

or pharmaceutically acceptable salt, ester, or salt of ester thereof;

wherein R_1 is hydrogen, aliphatic, heteroaliphatic, alicyclic, heteroalicyclic, aryl or heteroaryl;

R_2 and R_3 are each independently hydrogen, halogen, hydroxyl, protected hydroxyl, or an aliphatic, heteroaliphatic, alicyclic, heteroalicyclic, aryl or heteroaryl moiety; or

R_1 and R_2, when taken together, may form a substituted or unsubstituted, saturated or unsaturated cyclic ring of 3 to 8 carbon atoms; or

R_1 and R_3, when taken together, may form a substituted or unsubstituted, saturated or unsaturated cyclic ring of 3 to 8 carbon atoms;

R_4 is hydrogen or halogen;

R_5 is hydrogen, an oxygen protecting group or a prodrug;

R_6 is hydrogen, hydroxyl, or protected hydroxyl;

n is 0-2;

R_7, for each occurrence, is independently hydrogen, hydroxyl, or protected hydroxyl;

R_8 is hydrogen, halogen, hydroxyl, protected hydroxyl, alkyloxy, or an aliphatic moiety optionally substituted with hydroxyl, protected hydroxyl, SR_{12}, or $NR_{12}R_{13}$;

R_9 is hydrogen, halogen, hydroxyl, protected hydroxyl, OR_{12}, SR_{12}, $NR_{12}R_{13}$, $-X_1(CH_2)_pX_2-R_{14}$, or is C_{1-6}alkyl optionally substituted with hydroxyl, protected hydroxyl, halogen, amino, protected amino, or $-X_1(CH_2)_pX_2-R_{14}$;

wherein R_{12} and R_{13} are, independently for each occurrence, hydrogen, aliphatic, heteroaliphatic, alicyclic, heteroalicyclic, aryl or heteroaryl; or a protecting group, or R_{12} and R_{13}, taken together may form a saturated or unsaturated cyclic ring containing 1 to 4 carbon atoms and 1 to 3 nitrogen or oxygen atoms, and each of R_{12} and R_{13} are optionally further substituted with one or more occurrences of hydroxyl, protected hydroxyl, alkyloxy, amino, protected amino, alkylamino, aminoalkyl, or halogen,

wherein X_1 and X_2 are each independently absent, or are oxygen, NH, or -N(alkyl), or wherein X_2-R_{14} together are N_3 or are a saturated or unsaturated heterocyclic moiety,

p is 2-10, and

R_{14} is hydrogen, or an aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, or is – $(C=O)NHR_{15}$ –$(C=O)OR_{15}$, or –$(C=O)R_{15}$, wherein each occurrence of R_{15} is independently hydrogen, aliphatic, heteroaliphatic, alicyclic, heteroalicyclic, aryl or heteroaryl; or R_{14} is $–SO_2(R_{16})$, wherein R_{16} is an aliphatic moiety, wherein one or more of R_{14}, R_{15}, or R_{16} are optionally substituted with one or more occurrences of hydroxyl, protected hydroxyl, alkyloxy, amino, protected amino, alkylamino, aminoalkyl, or halogen; or

R_8 and R_9 may, when taken together, form a saturated or unsaturated cyclic ring containing 1 to 4 carbon atoms and 1 to 3 nitrogen or oxygen atoms and is optionally substituted with hydroxyl, protected hydroxyl, alkyloxy, amino, protected amino, alkylamino, aminoalkyl, or halogen;

R_{10} is hydrogen, hydroxyl, protected hydroxyl, amino, or protected amino;

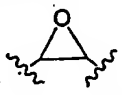
R_{11} is hydrogen, hydroxyl or protected hydroxyl;

X is absent or is O, NH, N-alkyl, CH_2 or S;

Y is CHR_{17}, O, C=O, CR_{17} or NR_{17}; and Z is CHR_{18}, O, C=O, CR_{18} or NR_{18}, wherein each occurrence of R_{17} and R_{18} is independently hydrogen or aliphatic, or R_{17} and R_{18} taken together is –O-, $-CH_2-$ or $-NR_{19}-$, wherein R_{19} is hydrogen or C_{1-6}alkyl, and Y and Z may be connected by a single or double bond;

with the proviso that when n is 1; X is O; R_1 is methyl; R_2, R_3, R_7 and R_{11} are each hydrogen; R_5 is hydrogen, C_{1-4}alkyl or $–C(=O)C_{1-4}$alkyl; R_6 is hydrogen, OH, C_{1-4}alkoxy or $–OC(=O)C_{1-4}$alkyl; and R_9 is OH, C_{1-4}alkoxy or $–OC(=O)C_{1-4}$alkyl; then one or more if the following groups do not occur simultaneously as defined:

(i) R_4 is hydrogen; R_{10} and R_8 are independently OH, C_{1-4}alkoxy or –OC(=O)C_{1-4}alkyl; and Y-Z is $–CH_2CH_2-$ or –CH=CH-;

(ii) R_4 and R_8 are each hydrogen; R_{10} is OH, C_{1-4}alkoxy or –OC(=O)C_{1-4}alkyl; and Y-Z is $–CHR^YCHR^Z-$, –CH=CH- or  ; wherein R^Y and R^Z are independently hydrogen, C_{1-4}alkyl or C_{1-4}alkanoyl; and

(iii) R_4 and R_{10} are each hydrogen, OH, C_{1-4}alkoxy or –OC(=O)C_{1-4}alkyl; R_8 is hydrogen, OH, halogen, C_{1-4}alkoxy or –OC(=O)C_{1-4}alkyl; and Y-Z is $–CH_2CH_2-$, –CH=CH- or $–C(=O)CH_2-$.

2. The compound of claim 1, where the following groups do not occur simultaneously as defined:

X is oxygen,

R_1 is methyl,

R_2 and R_3 are each hydrogen,

R_4 is hydrogen,

R_5 is hydrogen, C_{1-6}alkyl or C_{1-6}alkanoyl,

R_6 is OR', where R' is hydrogen, C_{1-6}alkyl or C_{1-6}alkanoyl with S-configuration,

R_7 is hydrogen,

Y and Z together represent $–CHR_{17}-CHR_{18}-$or $–CR_{17}=CR_{18}-$, wherein R_{17} and R_{18} are independently hydrogen, or when Y and Z are $–CHR_{17}-CHR_{18}-$, R_{17} and R_{18} taken together are –O-;

R_8 is hydrogen or OR', where R' is hydrogen, C_{1-6}alkyl or C_{1-6}alkanoyl,

R_9 is OR', where R' is hydrogen, C_{1-6}alkyl or C_{1-6}alkanoyl,

R_{10} is OR", where R" is hydrogen, C_{1-6}alkyl or C_{1-6}alkanoyl; and

R^{11} is hydrogen.

3. The compound of claim 1, wherein:

R_1 is hydrogen, straight or branched C_{1-6}alkyl, straight or branched C_{1-6}heteroalkyl, or aryl,

wherein the alkyl, heteroalkyl, and aryl groups may optionally be substituted with one or more occurrences of halogen, hydroxyl or protected hydroxyl;

R_2 and R_3 are each independently hydrogen, halogen, hydroxyl, protected hydroxyl, straight or branched C_{1-6}alkyl, straight or branched C_{1-6}heteroalkyl, or aryl, wherein the alkyl, heteroalkyl, and aryl groups may optionally be substituted with one or more occurrences of halogen, hydroxyl or protected hydroxyl; or

R_1 and R_2, when taken together, may form a saturated or unsaturated cyclic ring of 3 to 8 carbon atoms, optionally substituted with one or more occurrences of halogen; or

R_1 and R_3, when taken together, may form a saturated or unsaturated cyclic ring of 3 to 8 carbon atoms, optionally substituted with one or more occurrences of halogen;

R_4 is hydrogen or halogen;

R_5 is hydrogen or a protecting group;

R_6 is hydrogen, hydroxyl, or protected hydroxyl;

n is 0-2;

R_7, for each occurrence, is independently hydrogen, hydroxyl, or protected hydroxyl;

R_8 is hydrogen, halogen, hydroxyl, protected hydroxyl, alkyloxy, or C_{1-6}alkyl optionally substituted with hydroxyl, protected hydroxyl, SR_{12}, or $NR_{12}R_{13}$;

R_9 is hydrogen, halogen, hydroxyl, protected hydroxyl, OR_{12}, SR_{12}, $NR_{12}R_{13}$, $-X_1(CH_2)_pX_2-R_{14}$, or is C_{1-6}alkyl optionally substituted with hydroxyl, protected hydroxyl, halogen, amino, protected amino, or $-X_1(CH_2)_pX_2-R_{14}$;

wherein R_{12} and R_{13} are, independently for each occurrence, hydrogen, C_{1-6}alkyl, aryl, heteroaryl, alkylaryl, or alkylheteroaryl, or a protecting group, or R_{12} and R_{13}, taken together may form a saturated or unsaturated cyclic ring containing 1 to 4 carbon atoms and 1 to 3 nitrogen or oxygen atoms, and each of R_{12} and R_{13} are optionally further substituted with one or more occurrences of hydroxyl, protected hydroxyl, alkyloxy, amino, protected amino, alkylamino, aminoalkyl, or halogen,

wherein X_1 and X_2 are each independently absent, or are oxygen, NH, or -N(alkyl), or wherein X_2-R_{14} together are N_3 or are a saturated or unsaturated heterocyclic moiety,

p is 2-10, and

R_{14} is hydrogen, or an aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, or is $-(C=O)NHR_{15}$ $-(C=O)OR_{15}$, or $-(C=O)R_{15}$, wherein each occurrence of R_{15} is independently hydrogen, alkyl, heteroalkyl, aryl, heteroaryl, alkylaryl, or alkylheteroaryl, or R_{14} is $-SO_2(R_{16})$, wherein R_{16} is an alkyl moiety, wherein one or more of R_{14}, R_{15}, or R_{16} are optionally substituted with one or more occurrences of hydroxyl, protected hydroxyl, alkyloxy, amino, protected amino, alkylamino, aminoalkyl, or halogen; or

R_8 and R_9 may, when taken together, form a saturated or unsaturated cyclic ring containing 1 to 4 carbon atoms and 1 to 3 nitrogen or oxygen atoms and is optionally substituted with hydroxyl, protected hydroxyl, alkyloxy, amino, protected amino, alkylamino, aminoalkyl, or halogen;

R_{10} is hydrogen, hydroxyl, protected hydroxyl, amino, or protected amino;

R_{11} is hydrogen, hydroxyl or protected hydroxyl;

X is absent or is O, NH, N-alkyl, CH_2 or S;

Y is CHR_{17}, O, C=O, CR_{17} or NR_{17}; and Z is CHR_{18}, O, C=O, CR_{18} or NR_{18}, wherein each occurrence of R_{17} and R_{18} is independently hydrogen or C_{1-6}alkyl, or R_{17} and R_{18} taken together is –O-, $-CH_2-$ or $-NR_{19}-$, wherein R_{19} is hydrogen or C_{1-6}alkyl, and Y and Z may be connected by a single or double bond.

4. The compound of claim 3, where X is oxygen and n is 1.

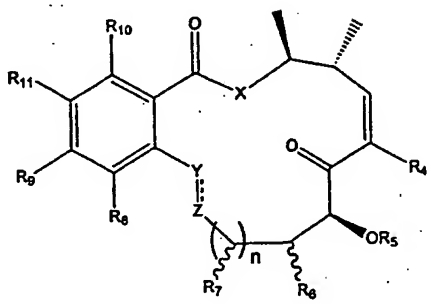
5. The compound of claim 3, where R_4 is halogen.

6. The compound of claim 3, where R_4 is fluorine.

7. The compound of claim 3, where Y and Z together represent-CH=CH-

8. The compound of claim 3, where Y and Z together represent trans –CH=CH-.

9. The compound of claim 3, wherein R_1 and R_2 are each methyl and R_3 is hydrogen and the compound has the structure:



wherein R_4-R_{11}, n, X, Y and Z are as defined in claim 3.

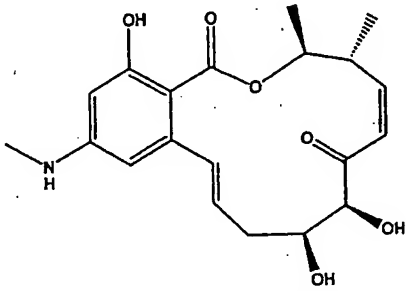
10. The compound of claim 9, wherein X is oxygen and n is 1.

11. The compound of claim 9, wherein R_4 is halogen.

20. The compound of claim 15, wherein X is oxygen, n is 1, R_1 and R_2 are each methyl, R_3 is hydrogen, R_4 is halogen, and Y and Z together represent –CH=CH-.

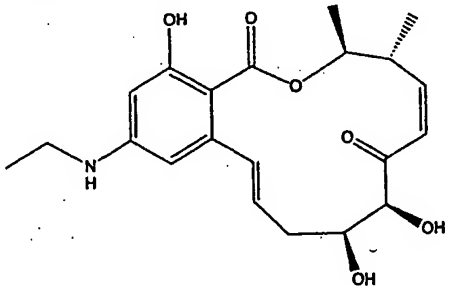
21. The compound of claim 18 or 20, wherein –CH=CH- is trans.

22. A compound having the structure:



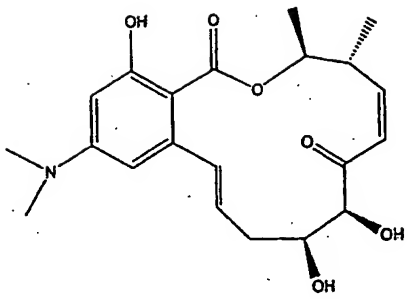
or pharmaceutically acceptable salt, ester, or salt of ester thereof.

23. A compound having the structure:



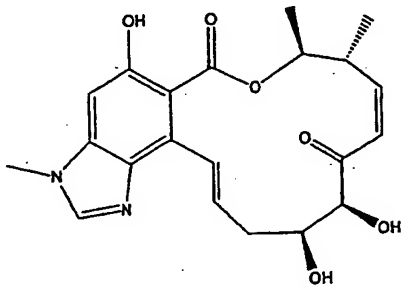
or pharmaceutically acceptable salt, ester, or salt of ester thereof.

24. A compound having the structure:



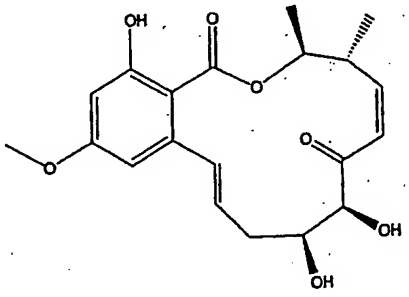
or pharmaceutically acceptable salt, ester, or salt of ester thereof.

25. A compound having the structure:



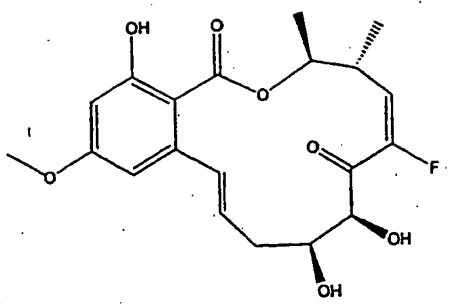
or pharmaceutically acceptable salt, ester, or salt of ester thereof.

26. A compound having the structure:



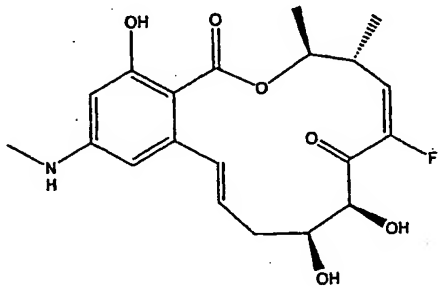
or pharmaceutically acceptable salt, ester, or salt of ester thereof.

27. A compound having the structure:



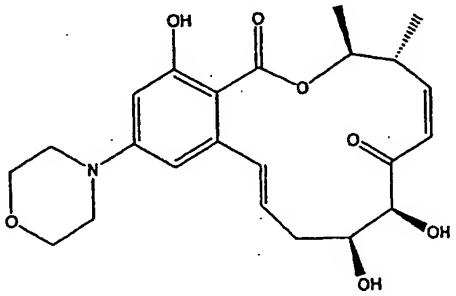
or pharmaceutically acceptable salt, ester, or salt of ester thereof.

28. A compound having the structure:



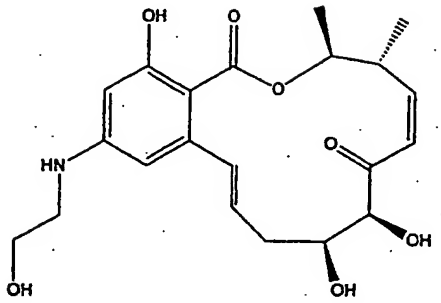
or pharmaceutically acceptable salt, ester, or salt of ester thereof.

29. A compound having the structure:



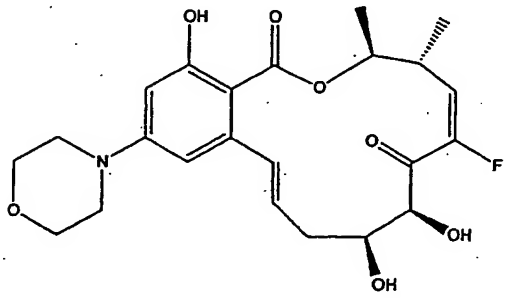
or pharmaceutically acceptable salt, ester, or salt of ester thereof.

30. A compound having the structure:



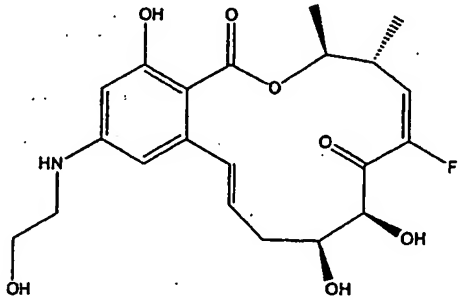
or pharmaceutically acceptable salt, ester, or salt of ester thereof.

31. A compound having the structure:



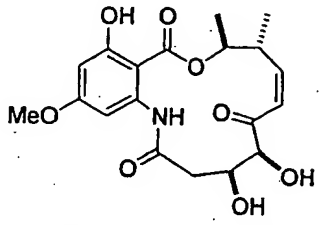
or pharmaceutically acceptable salt, ester, or salt of ester thereof.

32. A compound having the structure:



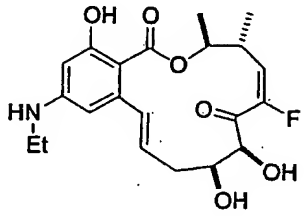
or pharmaceutically acceptable salt, ester, or salt of ester thereof.

33. A compound having the structure:



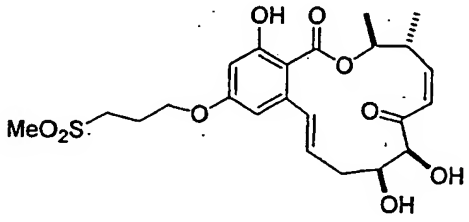
or pharmaceutically acceptable salt, ester, or salt of ester thereof.

34. A compound having the structure:



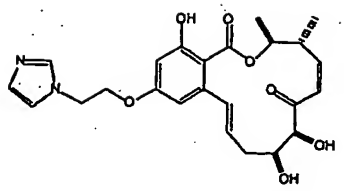
or pharmaceutically acceptable salt, ester, or salt of ester thereof.

35. A compound having the structure:



or pharmaceutically acceptable salt, ester, or salt of ester thereof.

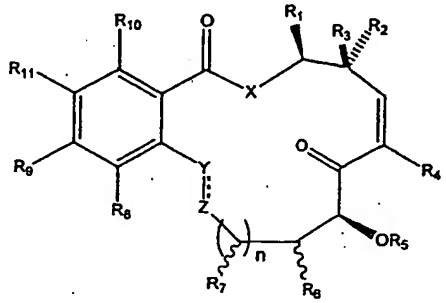
36. A compound having the structure:



or pharmaceutically acceptable salt, ester, or salt of ester thereof.

37. A pharmaceutical composition comprising:

a compound having the structure:



(I)

or pharmaceutically acceptable salt, ester, or salt of ester thereof;

wherein R_1 is hydrogen, aliphatic, heteroaliphatic, alicyclic, heteroalicyclic, aryl or heteroaryl;

R_2 and R_3 are each independently hydrogen, halogen, hydroxyl, protected hydroxyl, or an aliphatic, heteroaliphatic, alicyclic, heteroalicyclic, aryl or heteroaryl moiety; or

R_1 and R_2, when taken together, may form a substituted or unsubstituted, saturated or unsaturated cyclic ring of 3 to 8 carbon atoms; or

R_1 and R_3, when taken together, may form a substituted or unsubstituted, saturated or unsaturated cyclic ring of 3 to 8 carbon atoms;

R_4 is hydrogen or halogen;

R_5 is hydrogen, an oxygen protecting group or a prodrug;

R_6 is hydrogen, hydroxyl, or protected hydroxyl;

n is 0-2;

R_7, for each occurrence, is independently hydrogen, hydroxyl, or protected hydroxyl;

R_8 is hydrogen, halogen, hydroxyl, protected hydroxyl, alkyloxy, or an aliphatic moiety optionally substituted with hydroxyl, protected hydroxyl, SR_{12}, or $NR_{12}R_{13}$;

R_9 is hydrogen, halogen, hydroxyl, protected hydroxyl, OR_{12}, SR_{12}, $NR_{12}R_{13}$, $-X_1(CH_2)_pX_2-R_{14}$, or is C_{1-6}alkyl optionally substituted with hydroxyl, protected hydroxyl, halogen, amino, protected amino, or $-X_1(CH_2)_pX_2-R_{14}$;

wherein R_{12} and R_{13} are, independently for each occurrence, hydrogen, aliphatic, heteroaliphatic, alicyclic, heteroalicyclic, aryl or heteroaryl; or a protecting group, or R_{12} and R_{13}, taken together may form a saturated or unsaturated cyclic ring containing 1 to 4 carbon atoms and 1 to 3 nitrogen or oxygen atoms, and each of R_{12} and R_{13} are optionally further substituted with one or more occurrences of hydroxyl, protected hydroxyl, alkyloxy, amino, protected amino, alkylamino, aminoalkyl, or halogen,

wherein X_1 and X_2 are each independently absent, or are oxygen, NH, or -N(alkyl), or wherein X_2-R_{14} together are N_3 or are a saturated or unsaturated heterocyclic moiety,

p is 2-10, and

R_{14} is hydrogen, or an aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, or is $-(C=O)NHR_{15}$ $-(C=O)OR_{15}$, or $-(C=O)R_{15}$, wherein each occurrence of R_{15} is independently hydrogen, aliphatic, heteroaliphatic, alicyclic, heteroalicyclic, aryl or heteroaryl; or R_{14} is $-SO_2(R_{16})$, wherein R_{16} is an aliphatic moiety, wherein one or more of R_{14}, R_{15}, or R_{16} are optionally substituted with one or more occurrences of hydroxyl, protected hydroxyl, alkyloxy, amino, protected amino, alkylamino, aminoalkyl, or halogen; or

R_8 and R_9 may, when taken together, form a saturated or unsaturated cyclic ring containing 1 to 4 carbon atoms and 1 to 3 nitrogen or oxygen atoms and is optionally substituted with hydroxyl, protected hydroxyl, alkyloxy, amino, protected amino, alkylamino, aminoalkyl, or halogen;

R_{10} is hydrogen, hydroxyl, protected hydroxyl, amino, or protected amino;

R_{11} is hydrogen, hydroxyl or protected hydroxyl;

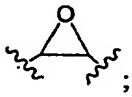
X is absent or is O, NH, N-alkyl, CH_2 or S;

Y is CHR_{17}, O, C=O, CR_{17} or NR_{17}; and Z is CHR_{18}, O, C=O, CR_{18} or NR_{18}, wherein each occurrence of R_{17} and R_{18} is independently hydrogen or aliphatic, or R_{17} and R_{18} taken together is –O-, $-CH_2-$ or $-NR_{19}-$, wherein R_{19} is hydrogen or C_{1-6}alkyl, and Y and Z may be connected by a single or double bond; and

a pharmaceutically acceptable carrier;

with the proviso that when n is 1; X is O; R_1 is methyl; R_2, R_3, R_7 and R_{11} are each hydrogen; R_5 is hydrogen, C_{1-4}alkyl or $-C(=O)C_{1-4}$alkyl; R_6 is hydrogen, OH, C_{1-4}alkoxy or $-OC(=O)C_{1-4}$alkyl; and R_9 is OH, C_{1-4}alkoxy or $-OC(=O)C_{1-4}$alkyl; then one or more if the following groups do not occur simultaneously as defined:

(i) R_4 is hydrogen; R_{10} and R_8 are independently OH, C_{1-4}alkoxy or $-OC(=O)C_{1-4}$alkyl; and Y-Z is $-CH_2CH_2-$ or –CH=CH-;

(ii) R_4 and R_8 are each hydrogen; R_{10} is OH, C_{1-4}alkoxy or $-OC(=O)C_{1-4}$alkyl; and Y-Z is $-CHR^YCHR^Z-$, –CH=CH- or  ; wherein R^Y and R^Z are independently hydrogen, C_{1-4}alkyl or C_{1-4}alkanoyl; and

(iii) R_4 and R_{10} are each hydrogen, OH, C_{1-4}alkoxy or $-OC(=O)C_{1-4}$alkyl; R_8 is hydrogen, OH, halogen, C_{1-4}alkoxy or $-OC(=O)C_{1-4}$alkyl; and Y-Z is $-CH_2CH_2-$, –CH=CH- or $-C(=O)CH_2-$.

38. The pharmaceutical composition of claim 37, wherein the compound is present in an amount effective to inhibit NF-κB activation.

39. The pharmaceutical composition of claim 37, wherein the compound is present in an amount effective to inhibit AP-1 activation.

40. The pharmaceutical composition of claim 37, wherein the compound is present in an amount effective to inhibit a protein kinase.

41. The pharmaceutical composition of claim 39, wherein the protein kinase is MEKK1, MEK1, VEGFr or PDGFr.

42. The pharmaceutical composition of claim 37, wherein the compound is present in an amount effective to inhibit proliferation of cancerous cells and angiogenesis on solid tumors.

43. The pharmaceutical composition of claim 37, wherein the compound is present in an amount effective to have an anti-inflammatory effect.

44. The pharmaceutical composition of claim 37, wherein the compound is present in an amount effective to treat psoriasis.

45. The pharmaceutical composition of claim 37, wherein the compound is present in an amount effective to reduce skin photodamage.

46. The pharmaceutical composition of claim 37, wherein the compound is present in an amount effective to prevent restenosis.

47. The pharmaceutical composition of claim 37, where:

R_1 is hydrogen, straight or branched C_{1-6}alkyl, straight or branched C_{1-6}heteroalkyl, or aryl,

wherein the alkyl, heteroalkyl, and aryl groups may optionally be substituted with one or more occurrences of halogen, hydroxyl or protected hydroxyl;

R_2 and R_3 are each independently hydrogen, halogen, hydroxyl, protected hydroxyl, straight or branched C_{1-6}alkyl, straight or branched C_{1-6}heteroalkyl, or aryl,

wherein the alkyl, heteroalkyl, and aryl groups may optionally be substituted with one or more occurrences of halogen, hydroxyl or protected hydroxyl; or

R_1 and R_2, when taken together, may form a saturated or unsaturated cyclic ring of 3 to 8 carbon atoms, optionally substituted with one or more occurrences of halogen; or

R_1 and R_3, when taken together, may form a saturated or unsaturated cyclic ring of 3 to 8 carbon atoms, optionally substituted with one or more occurrences of halogen;

R_4 is hydrogen or halogen;

R_5 is hydrogen or a protecting group;

R_6 is hydrogen, hydroxyl, or protected hydroxyl;

n is 0-2;

R_7, for each occurrence, is independently hydrogen, hydroxyl, or protected hydroxyl;

R_8 is hydrogen, halogen, hydroxyl, protected hydroxyl, alkyloxy, or C_{1-6}alkyl optionally substituted with hydroxyl, protected hydroxyl, SR_{12}, or $NR_{12}R_{13}$;

R_9 is hydrogen, halogen, hydroxyl, protected hydroxyl, OR_{12}, SR_{12}, $NR_{12}R_{13}$, $-X_1(CH_2)_pX_2-R_{14}$, or is C_{1-6}alkyl optionally substituted with hydroxyl, protected hydroxyl, halogen, amino, protected amino, or $-X_1(CH_2)_pX_2-R_{14}$;

wherein R_{12} and R_{13} are, independently for each occurrence, hydrogen, C_{1-6}alkyl, aryl, heteroaryl, alkylaryl, or alkylheteroaryl, or a protecting group, or R_{12} and R_{13}, taken together may form a saturated or unsaturated cyclic ring containing 1 to 4 carbon atoms and 1 to 3 nitrogen or oxygen atoms, and each of R_{12} and R_{13} are optionally further substituted with one or more occurrences of hydroxyl, protected hydroxyl, alkyloxy, amino, protected amino, alkylamino, aminoalkyl, or halogen,

wherein X_1 and X_2 are each independently absent, or are oxygen, NH, or -N(alkyl), or wherein X_2-R_{14} together are N_3 or are a saturated or unsaturated heterocyclic moiety,

p is 2-10, and

R_{14} is hydrogen, or an aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, or is $-(C=O)NHR_{15}$ $-(C=O)OR_{15}$, or $-(C=O)R_{15}$, wherein each occurrence of R_{15} is independently hydrogen, alkyl, heteroalkyl, aryl, heteroaryl, alkylaryl, or alkylheteroaryl, or R_{14} is $-SO_2(R_{16})$, wherein R_{16} is an alkyl moiety, wherein one or more of R_{14}, R_{15}, or R_{16} are optionally substituted with one or more occurrences of hydroxyl, protected hydroxyl, alkyloxy, amino, protected amino, alkylamino, aminoalkyl, or halogen; or

R_8 and R_9 may, when taken together, form a saturated or unsaturated cyclic ring containing 1 to 4 carbon atoms and 1 to 3 nitrogen or oxygen atoms and is optionally substituted with hydroxyl, protected hydroxyl, alkyloxy, amino, protected amino, alkylamino, aminoalkyl, or halogen;

R_{10} is hydrogen, hydroxyl, protected hydroxyl, amino, or protected amino;

R_{11} is hydrogen, hydroxyl or protected hydroxyl;

X is absent or is O, NH, N-alkyl, CH_2 or S;

Y is CHR_{17}, O, C=O, CR_{17} or NR_{17}; and Z is CHR_{18}, O, C=O, CR_{18} or NR_{18}, wherein each occurrence of R_{17} and R_{18} is independently hydrogen or C_{1-6}alkyl, or R_{17} and R_{18} taken together is –O-, -CH_2- or -NR_{19}-, wherein R_{19} is hydrogen or C_{1-6}alkyl, and Y and Z may be connected by a single or double bond.

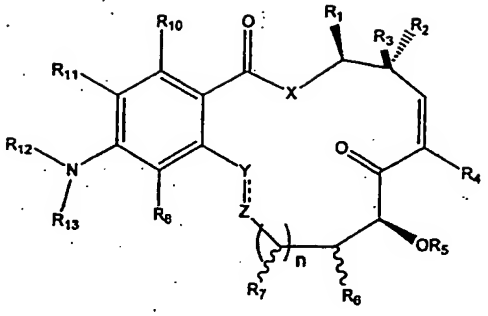
48. The pharmaceutical composition of claim 47, where X is oxygen and n is 1.

49. The pharmaceutical composition of claim 47, where R_4 is halogen.

50. The pharmaceutical composition of claim 49, where R_4 is fluorine.

51. The pharmaceutical composition of claim 47, where Y and Z together represent – CH=CH-.

52. The pharmaceutical composition of claim 51, wherein –CH=CH- is trans.



wherein R_1-R_{13}, n, X, Y and Z are as defined in claim 46, or

R_{13} and R_8 may, when taken together, form a cyclic ring containing 1 to 4 carbon atoms and 1 to 3 nitrogen or oxygen atoms and is optionally substituted with hydrogen, alkyloxy, amino, alkylamino, aminoalkyl, and halogen.

60. The pharmaceutical composition of claim 59, wherein X is oxygen and n is 1.

61. The pharmaceutical composition of claim 59, wherein R_4 is halogen.

62. The pharmaceutical composition of claim 59, wherein Y and Z together represent – CH=CH-.

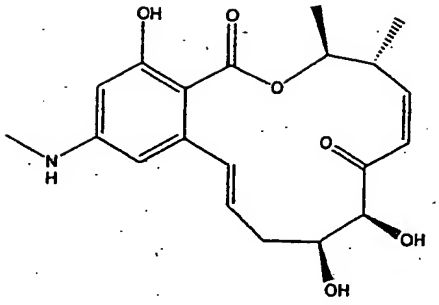
63. The pharmaceutical composition of claim 59, wherein R_1 and R_2 are each methyl and R_3 is hydrogen.

64. The pharmaceutical composition of claim 59 wherein X is oxygen, n is 1, R_1 and R_2 are each methyl, R_3 is hydrogen, R_4 is halogen, and Y and Z together represent –CH=CH-.

65. The pharmaceutical composition of claim 63 or 64 wherein –CH=CH- is trans.

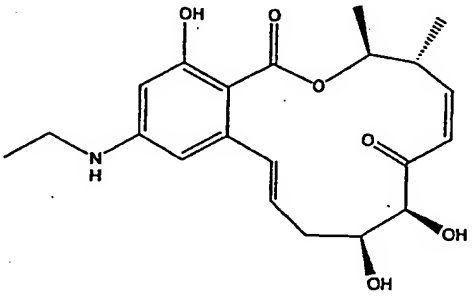
66. A pharmaceutical composition comprising:

a compound having the structure:



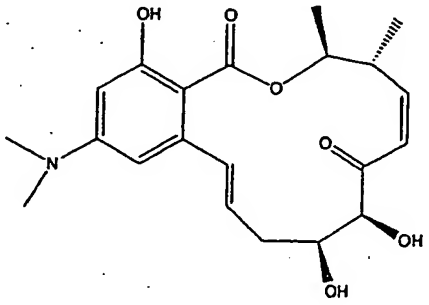
or pharmaceutically acceptable salt, ester, or salt of ester thereof; and
a pharmaceutically acceptable carrier.

67. A pharmaceutical composition comprising:
a compound having the structure:



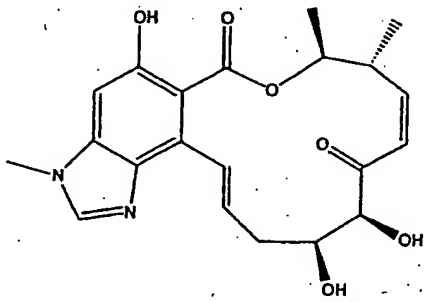
or pharmaceutically acceptable salt, ester, or salt of ester thereof; and
a pharmaceutically acceptable carrier.

68. A pharmaceutical composition comprising:
a compound having the structure:



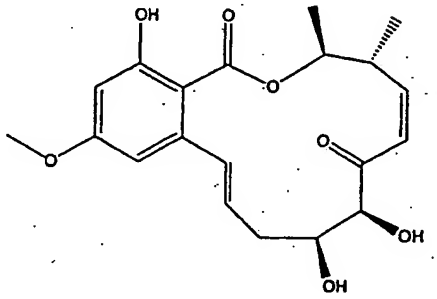
or pharmaceutically acceptable salt, ester, or salt of ester thereof; and
a pharmaceutically acceptable carrier.

69. A pharmaceutical composition comprising:
a compound having the structure:



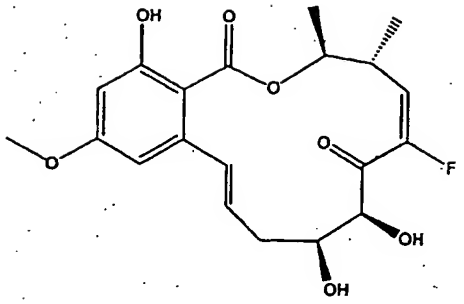
or pharmaceutically acceptable salt, ester, or salt of ester thereof; and
a pharmaceutically acceptable carrier.

70. A pharmaceutical composition comprising:
a compound having the structure:



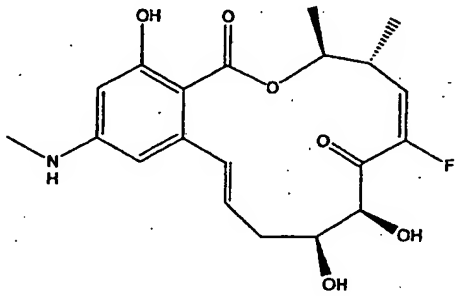
or pharmaceutically acceptable salt, ester, or salt of ester thereof; and
a pharmaceutically acceptable carrier.

71. A pharmaceutical composition comprising:
a compound having the structure:



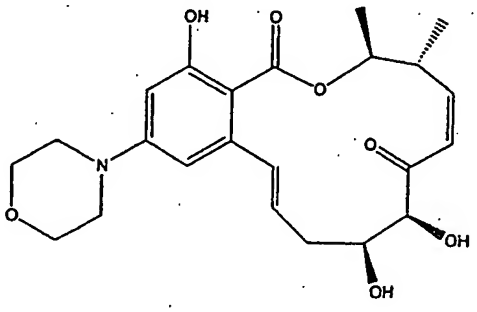
or pharmaceutically acceptable salt, ester, or salt of ester thereof; and
a pharmaceutical acceptable carrier.

72. A pharmaceutical composition comprising:
a compound having the structure:



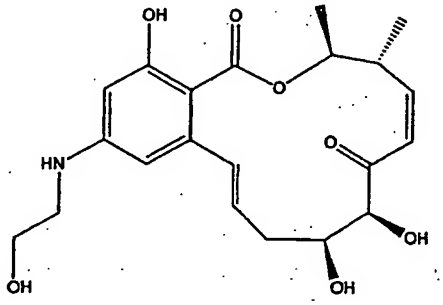
or pharmaceutically acceptable salt, ester, or salt of ester thereof; and
a pharmaceutical acceptable carrier.

73. A pharmaceutical composition comprising:
a compound having the structure:



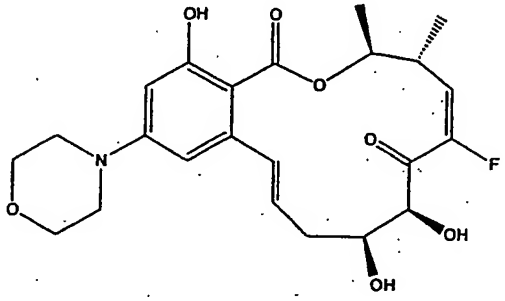
or pharmaceutically acceptable salt, ester, or salt of ester thereof; and
a pharmaceutically acceptable carrier.

74. A pharmaceutical composition comprising:
a compound having the structure:



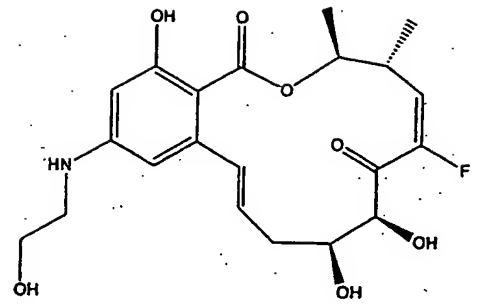
or pharmaceutically acceptable salt, ester, or salt of ester thereof; and
a pharmaceutically acceptable carrier.

75. A pharmaceutical composition comprising:
a compound having the structure:



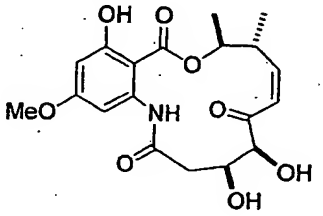
or pharmaceutically acceptable salt, ester, or salt of ester thereof; and
a pharmaceuticlaly acceptable carrier.

76. A pharmaceutical composition comprising:
a compound having the structure:



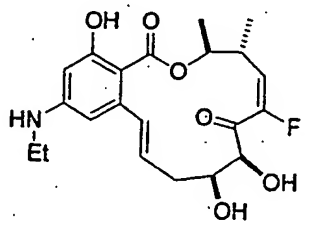
or pharmaceutically acceptable salt, ester, or salt of ester thereof; and
a pharmaceutically acceptable carrier.

77. A pharmaceutical composition comprising:
a compound having the structure:



or pharmaceutically acceptable salt, ester, or salt of ester thereof; and
a pharmaceutically acceptable carrier.

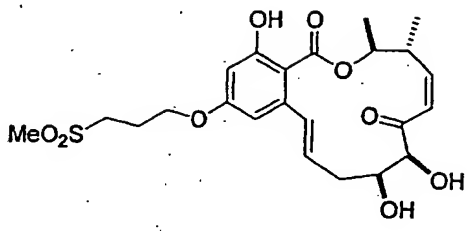
78. A pharmaceutical composition comprising:
a compound having the structure:



or pharmaceutically acceptable salt, ester, or salt of ester thereof; and
a pharmaceutically acceptable carrier.

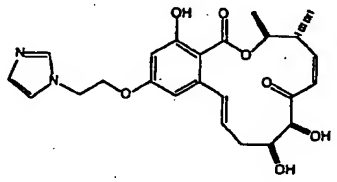
79. A pharmaceutical composition comprising:

a compound having the structure:



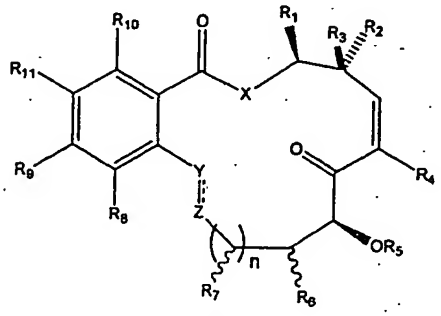
or pharmaceutically acceptable salt, ester, or salt of ester thereof; and
a pharmaceutically acceptable carrier.

80. A pharmaceutical composition comprising:
a compound having the structure:



or pharmaceutically acceptable salt, ester, or salt of ester thereof; and
a pharmaceutically acceptable carrier.

81. A topical pharmaceutical composition for preventing or treating UVB-induced photodamage comprising:
a compound having the structure:



(I)

or pharmaceutically acceptable salt, ester, or salt of ester thereof;

wherein R_1 is hydrogen, straight or branched C_{1-6}alkyl, straight or branched C_{1-6}heteroalkyl, or aryl,

wherein the alkyl, heteroalkyl, and aryl groups may optionally be substituted with one or more occurrences of halogen, hydroxyl or protected hydroxyl;

R_2 and R_3 are each independently hydrogen, halogen, hydroxyl, protected hydroxyl, straight or branched C_{1-6}alkyl, straight or branched C_{1-6}heteroalkyl, or aryl,

wherein the alkyl, heteroalkyl, and aryl groups may optionally be substituted with one or more occurrences of halogen, hydroxyl or protected hydroxyl; or

R_1 and R_2, when taken together, may form a saturated or unsaturated cyclic ring of 3 to 8 carbon atoms, optionally substituted with one or more occurrences of halogen; or

R_1 and R_3, when taken together, may form a saturated or unsaturated cyclic ring of 3 to 8 carbon atoms, optionally substituted with one or more occurrences of halogen;

R_4 is hydrogen or halogen;

R_5 is hydrogen or a protecting group;

R_6 is hydrogen, hydroxyl, or protected hydroxyl;

n is 0-2;

R_7, for each occurrence, is independently hydrogen, hydroxyl, or protected hydroxyl;

R_8 is hydrogen, halogen, hydroxyl, protected hydroxyl, alkyloxy, or C_{1-6}alkyl optionally substituted with hydroxyl, protected hydroxyl, SR_{12}, or $NR_{12}R_{13}$;

R_9 is hydrogen, halogen, hydroxyl, protected hydroxyl, OR_{12}, SR_{12}, $NR_{12}R_{13}$, $-X_1(CH_2)_pX_2-R_{14}$, or is C_{1-6}alkyl optionally substituted with hydroxyl, protected hydroxyl, halogen, amino, protected amino, or $-X_1(CH_2)_pX_2-R_{14}$;

wherein R_{12} and R_{13} are, independently for each occurrence, hydrogen, C_{1-6}alkyl, aryl, heteroaryl, alkylaryl, or alkylheteroaryl, or a protecting group, or R_{12} and R_{13}, taken together may form a saturated or unsaturated cyclic ring containing 1 to 4 carbon atoms and 1 to 3 nitrogen or oxygen atoms, and each of R_{12} and R_{13} are optionally further substituted with one or more occurrences

of hydroxyl, protected hydroxyl, alkyloxy, amino, protected amino, alkylamino, aminoalkyl, or halogen,

wherein X_1 and X_2 are each independently absent, or are oxygen, NH, or -N(alkyl), or wherein X_2-R_{14} together are N_3 or are a saturated or unsaturated heterocyclic moiety,

p is 2-10, and

R_{14} is hydrogen, or an aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, or is $-(C=O)NHR_{15}$ $-(C=O)OR_{15}$, or $-(C=O)R_{15}$, wherein each occurrence of R_{15} is independently hydrogen, alkyl, heteroalkyl, aryl, heteroaryl, alkylaryl, or alkylheteroaryl, or R_{14} is $-SO_2(R_{16})$, wherein R_{16} is an alkyl moiety, wherein one or more of R_{14}, R_{15}, or R_{16} are optionally substituted with one or more occurrences of hydroxyl, protected hydroxyl, alkyloxy, amino, protected amino, alkylamino, aminoalkyl, or halogen; or

R_8 and R_9 may, when taken together, form a saturated or unsaturated cyclic ring containing 1 to 4 carbon atoms and 1 to 3 nitrogen or oxygen atoms and is optionally substituted with hydroxyl, protected hydroxyl, alkyloxy, amino, protected amino, alkylamino, aminoalkyl, or halogen;

R_{10} is hydrogen, hydroxyl, protected hydroxyl, amino, or protected amino;

R_{11} is hydrogen, hydroxyl or protected hydroxyl;

X is absent or is O, NH, N-alkyl, CH_2 or S;

Y is CHR_{17}, O, C=O, CR_{17} or NR_{17}; and Z is CHR_{18}, O, C=O, CR_{18} or NR_{18}, wherein each occurrence of R_{17} and R_{18} is independently hydrogen or $C_{1\text{-}6}$alkyl, or R_{17} and R_{18} taken together is –O-, $-CH_2-$ or $-NR_{19}-$, wherein R_{19} is hydrogen or $C_{1\text{-}6}$alkyl, and Y and Z may be connected by a single or double bond; and

a pharmaceutically acceptable carrier;

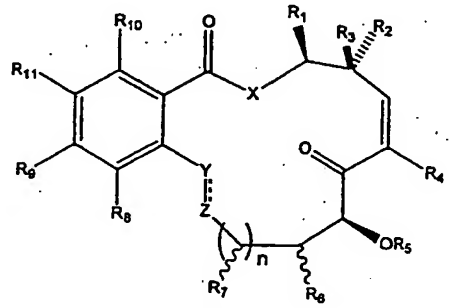
wherein the compound is present in an amount effective to prevent or treat UVB-induced photodamage.

82. The pharmaceutical composition of claim 81, further comprising a cosmetic ingredient.

83. The pharmaceutical composition of claim 82, wherein the cosmetic ingredient is a sunscreen.

84. A method for treating an inflammatory and/or autoimmune disorder or a disorder resulting from increased angiogenesis and/or cell proliferation comprising:

administering to a subject in need thereof a therapeutically effective amount of a compound having the structure:



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or pharmaceutically acceptable salt, ester, or salt of ester thereof;

wherein R_1 is hydrogen, aliphatic, heteroaliphatic, alicyclic, heteroalicyclic, aryl or heteroaryl;

R_2 and R_3 are each independently hydrogen, halogen, hydroxyl, protected hydroxyl, or an aliphatic, heteroaliphatic, alicyclic, heteroalicyclic, aryl or heteroaryl moiety; or

R_1 and R_2, when taken together, may form a substituted or unsubstituted, saturated or unsaturated cyclic ring of 3 to 8 carbon atoms; or

R_1 and R_3, when taken together, may form a substituted or unsubstituted, saturated or unsaturated cyclic ring of 3 to 8 carbon atoms;

R_4 is hydrogen or halogen;

R_5 is hydrogen, an oxygen protecting group or a prodrug;

R_6 is hydrogen, hydroxyl, or protected hydroxyl;

n is 0-2;

R_7, for each occurrence, is independently hydrogen, hydroxyl, or protected hydroxyl;

R_8 is hydrogen, halogen, hydroxyl, protected hydroxyl, alkyloxy, or an aliphatic moiety optionally substituted with hydroxyl, protected hydroxyl, SR_{12}, or $NR_{12}R_{13}$;

R_9 is hydrogen, halogen, hydroxyl, protected hydroxyl, OR_{12}, SR_{12}, $NR_{12}R_{13}$, $-X_1(CH_2)_pX_2-R_{14}$, or is C_{1-6}alkyl optionally substituted with hydroxyl, protected hydroxyl, halogen, amino, protected amino, or $-X_1(CH_2)_pX_2-R_{14}$;

wherein R_{12} and R_{13} are, independently for each occurrence, hydrogen, aliphatic, heteroaliphatic, alicyclic, heteroalicyclic, aryl or heteroaryl; or a protecting group, or R_{12} and R_{13}, taken together may form a saturated or unsaturated cyclic ring containing 1 to 4 carbon atoms and 1 to 3 nitrogen or oxygen atoms, and each of R_{12} and R_{13} are optionally further substituted with one or more occurrences of hydroxyl, protected hydroxyl, alkyloxy, amino, protected amino, alkylamino, aminoalkyl, or halogen,

wherein X_1 and X_2 are each independently absent, or are oxygen, NH, or -N(alkyl), or wherein X_2-R_{14} together are N_3 or are a saturated or unsaturated heterocyclic moiety,

p is 2-10, and

R_{14} is hydrogen, or an aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, or is $-(C=O)NHR_{15}$ $-(C=O)OR_{15}$, or $-(C=O)R_{15}$, wherein each occurrence of R_{15} is independently hydrogen, aliphatic, heteroaliphatic, alicyclic, heteroalicyclic, aryl or heteroaryl; or R_{14} is $-SO_2(R_{16})$, wherein R_{16} is an aliphatic moiety, wherein one or more of R_{14}, R_{15}, or R_{16} are optionally substituted with one or more occurrences of hydroxyl, protected hydroxyl, alkyloxy, amino, protected amino, alkylamino, aminoalkyl, or halogen; or

R_8 and R_9 may, when taken together, form a saturated or unsaturated cyclic ring containing 1 to 4 carbon atoms and 1 to 3 nitrogen or oxygen atoms and is optionally substituted with hydroxyl, protected hydroxyl, alkyloxy, amino, protected amino, alkylamino, aminoalkyl, or halogen;

R_{10} is hydrogen, hydroxyl, protected hydroxyl, amino, or protected amino;

R_{11} is hydrogen, hydroxyl or protected hydroxyl;

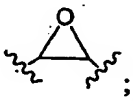
X is absent or is O, NH, N-alkyl, CH_2 or S;

Y is CHR_{17}, O, C=O, CR_{17} or NR_{17}; and Z is CHR_{18}, O, C=O, CR_{18} or NR_{18}, wherein each occurrence of R_{17} and R_{18} is independently hydrogen or aliphatic, or R_{17} and R_{18} taken together is –O-, $-CH_2-$ or $-NR_{19}-$, wherein R_{19} is hydrogen or C_{1-6}alkyl, and Y and Z may be connected by a single or double bond; and

a pharmaceutically acceptable carrier or diluent;

with the proviso that when n is 1; X is O; R_1 is methyl; R_2, R_3, R_7 and R_{11} are each hydrogen; R_5 is hydrogen, C_{1-4}alkyl or $-C(=O)C_{1-4}$alkyl; R_6 is hydrogen, OH, C_{1-4}alkoxy or $-OC(=O)C_{1-4}$alkyl; and R_9 is OH, C_{1-4}alkoxy or $-OC(=O)C_{1-4}$alkyl; then one or more if the following groups do not occur simultaneously as defined:

(i) R_4 is hydrogen; R_{10} and R_8 are independently OH, C_{1-4}alkoxy or $-OC(=O)C_{1-4}$alkyl; and Y-Z is $-CH_2CH_2-$ or $-CH=CH-$; and

(ii) R_4 and R_8 are each hydrogen; R_{10} is OH, C_{1-4}alkoxy or $-OC(=O)C_{1-4}$alkyl; and Y-Z is $-CHR^YCHR^Z-$, $-CH=CH-$ or  ; wherein R^Y and R^Z are independently hydrogen, C_{1-4}alkyl or C_{1-4}alkanoyl; and

(iii) R_4 and R_{10} are each hydrogen, OH, C_{1-4}alkoxy or $-OC(=O)C_{1-4}$alkyl; R_8 is hydrogen, OH, halogen, C_{1-4}alkoxy or $-OC(=O)C_{1-4}$alkyl; and Y-Z is $-CH_2CH_2-$, $-CH=CH-$ or $-C(=O)CH_2-$; whereby the compound induces mRNA degradation and the method is for treating a disorder resulting from cell proliferation.

85. The method of claim 84, wherein the method is for treating a disorder selected from the group consisting of rheumatoid arthritis, psoriasis, asthma, cancer, sepsis, inflammatory bowel disease, atopic dermatitis, Crohn's disease, and autoimmune disorders.

86. The method of claim 84, wherein the method is for treating rheumatoid arthritis.

87. The method of claim 84, wherein the method is for treating psoriasis.

88. The method of claim 84, wherein the method is for treating asthma.

89. The method of claim 84, wherein:

R_1 is hydrogen, straight or branched C_{1-6}alkyl, straight or branched C_{1-6}heteroalkyl, or aryl,

wherein the alkyl, heteroalkyl, and aryl groups may optionally be substituted with one or more occurrences of halogen, hydroxyl or protected hydroxyl;

R_2 and R_3 are each independently hydrogen, halogen, hydroxyl, protected hydroxyl, straight or branched C_{1-6}alkyl, straight or branched C_{1-6}heteroalkyl, or aryl,

wherein the alkyl, heteroalkyl, and aryl groups may optionally be substituted with one or more occurrences of halogen, hydroxyl or protected hydroxyl; or

R_1 and R_2, when taken together, may form a saturated or unsaturated cyclic ring of 3 to 8 carbon atoms, optionally substituted with one or more occurrences of halogen; or

R_1 and R_3, when taken together, may form a saturated or unsaturated cyclic ring of 3 to 8 carbon atoms, optionally substituted with one or more occurrences of halogen;

R_4 is hydrogen or halogen;

R_5 is hydrogen or a protecting group;

R_6 is hydrogen, hydroxyl, or protected hydroxyl;

n is 0-2;

R_7, for each occurrence, is independently hydrogen, hydroxyl, or protected hydroxyl;

R_8 is hydrogen, halogen, hydroxyl, protected hydroxyl, alkyloxy, or C_{1-6}alkyl optionally substituted with hydroxyl, protected hydroxyl, SR_{12}, or $NR_{12}R_{13}$;

R_9 is hydrogen, halogen, hydroxyl, protected hydroxyl, OR_{12}, SR_{12}, $NR_{12}R_{13}$, $-X_1(CH_2)_pX_2-R_{14}$, or is C_{1-6}alkyl optionally substituted with hydroxyl, protected hydroxyl, halogen, amino, protected amino, or $-X_1(CH_2)_pX_2-R_{14}$;

wherein R_{12} and R_{13} are, independently for each occurrence, hydrogen, C_{1-6}alkyl, aryl, heteroaryl, alkylaryl, or alkylheteroaryl, or a protecting group, or R_{12} and R_{13}, taken together may form a saturated or unsaturated cyclic ring containing 1 to 4 carbon atoms and 1 to 3 nitrogen or oxygen atoms, and each of R_{12} and R_{13} are optionally further substituted with one or more occurrences of hydroxyl, protected hydroxyl, alkyloxy, amino, protected amino, alkylamino, aminoalkyl, or halogen,

wherein X_1 and X_2 are each independently absent, or are oxygen, NH, or -N(alkyl), or wherein X_2-R_{14} together are N_3 or are a saturated or unsaturated heterocyclic moiety,

p is 2-10, and

R_{14} is hydrogen, or an aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, or is $-(C=O)NHR_{15}$ $-(C=O)OR_{15}$, or $-(C=O)R_{15}$, wherein each occurrence of R_{15} is independently hydrogen, alkyl, heteroalkyl, aryl, heteroaryl, alkylaryl, or alkylheteroaryl, or R_{14} is $-SO_2(R_{16})$, wherein R_{16} is an alkyl moiety, wherein one or more of R_{14}, R_{15}, or R_{16} are optionally substituted with one or more occurrences of hydroxyl, protected hydroxyl, alkyloxy, amino, protected amino, alkylamino, aminoalkyl, or halogen; or

R_8 and R_9 may, when taken together, form a saturated or unsaturated cyclic ring containing 1 to 4 carbon atoms and 1 to 3 nitrogen or oxygen atoms and is optionally substituted with hydroxyl, protected hydroxyl, alkyloxy, amino, protected amino, alkylamino, aminoalkyl, or halogen;

R_{10} is hydrogen, hydroxyl, protected hydroxyl, amino, or protected amino;

R_{11} is hydrogen, hydroxyl or protected hydroxyl;

X is absent or is O, NH, N-alkyl, CH_2 or S;

Y is CHR_{17}, O, C=O, CR_{17} or NR_{17}; and Z is CHR_{18}, O, C=O, CR_{18} or NR_{18}, wherein each occurrence of R_{17} and R_{18} is independently hydrogen or C_{1-6}alkyl, or R_{17} and R_{18} taken together is –O-, $-CH_2-$ or $-NR_{19}-$, wherein R_{19} is hydrogen or C_{1-6}alkyl, and Y and Z may be connected by a single or double bond.

90. The method of claim 89, wherein in the compound X is oxygen and n is 1.

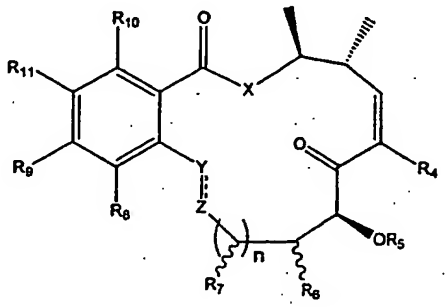
91. The method of claim 89, wherein in the compound R_4 is halogen.

92. The method of claim 89 is wherein in the compound R_4 is fluorine.

93. The method of claim 89, wherein in the compound Y and Z together represent-CH=CH-

94. The method of claim 93, wherein in the compound Y and Z together represent trans –CH=CH-.

95. The method of claim 89, comprising administering a compound wherein R_1 and R_2 are each methyl and R_3 is hydrogen and the compound has the structure:



wherein R_4-R_{11}, n, X, Y and Z are as defined in claim 88.

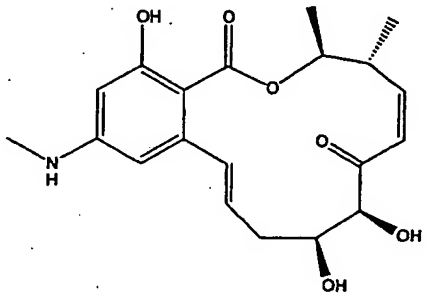
96. The method of claim 95, wherein in the compound X is oxygen and n is 1.

97. The method of claim 95, wherein in the compound R_4 is halogen.

106. The method of claim 101, wherein in the compound X is oxygen, n is 1, R_1 and R_2 are each methyl, R_3 is hydrogen, R_4 is halogen, and Y and Z together represent –CH=CH-.

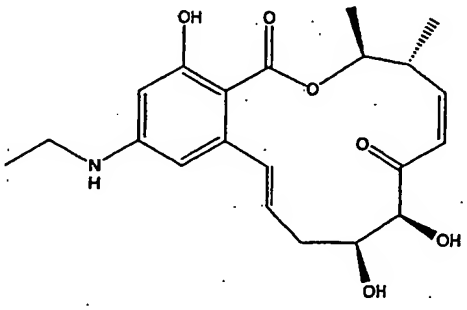
107. The method of claim 105 or 106, wherein in the compound –CH=CH- is trans.

108. The method of claim 84, comprising administering a compound having the structure:



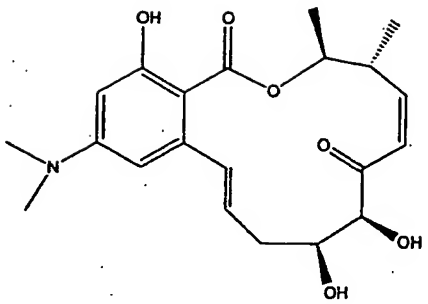
or pharmaceutically acceptable salt, ester, or salt of ester thereof.

109. The method of claim 84, comprising administering a compound having the structure:



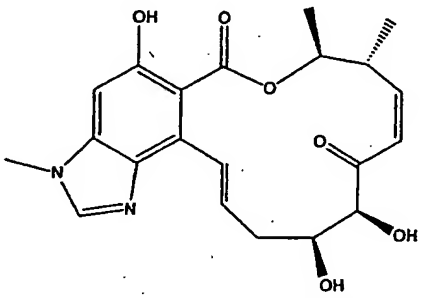
or pharmaceutically acceptable salt, ester, or salt of ester thereof.

110. The method of claim 84, comprising administering a compound having the structure:



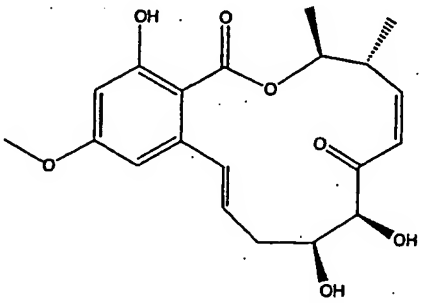
or pharmaceutically acceptable salt, ester, or salt of ester thereof.

111. The method of claim 84, comprising administering a compound having the structure:



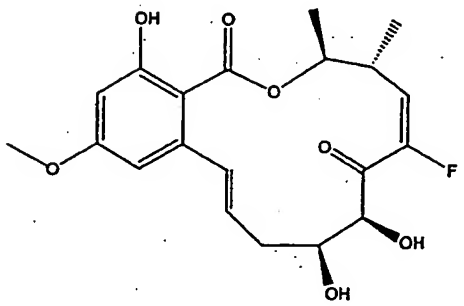
or pharmaceutically acceptable salt, ester, or salt of ester thereof.

112. The method of claim 84, comprising administering a compound having the structure:



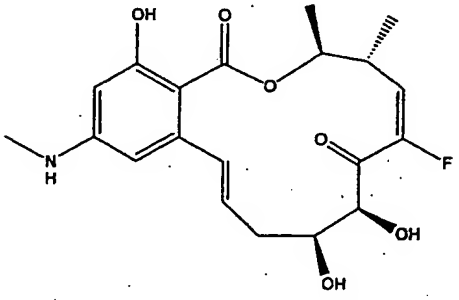
or pharmaceutically acceptable salt, ester, or salt of ester thereof.

113. The method of claim 84, comprising administering a compound having the structure:



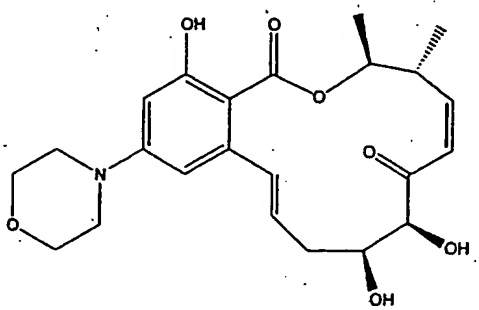
or pharmaceutically acceptable salt, ester, or salt of ester thereof.

114. The method of claim 84, comprising administering a compound having the structure:



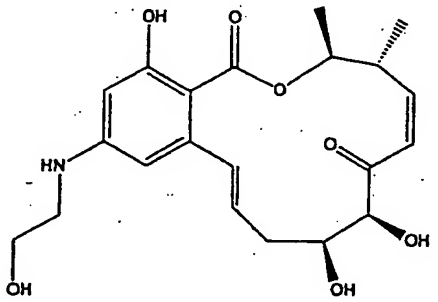
or pharmaceutically acceptable salt, ester, or salt of ester thereof.

115. The method of claim 84, comprising administering a compound having the structure:



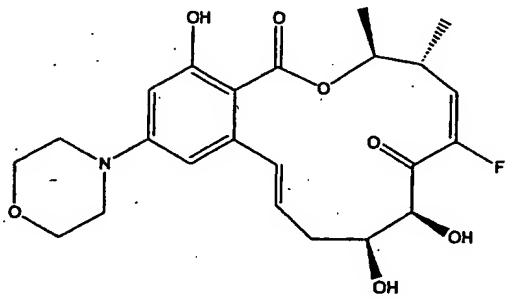
or pharmaceutically acceptable salt, ester, or salt of ester thereof.

116. The method of claim 84, comprising administering a compound having the structure:



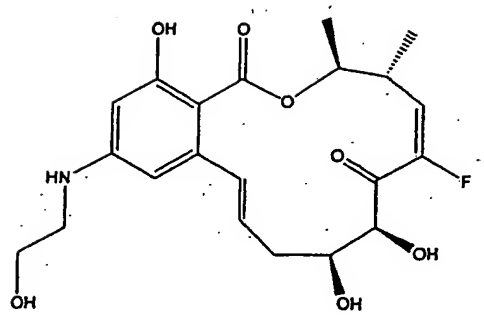
or pharmaceutically acceptable salt, ester, or salt of ester thereof.

117. The method of claim 84, comprising administering a compound having the structure:



or pharmaceutically acceptable salt, ester, or salt of ester thereof.

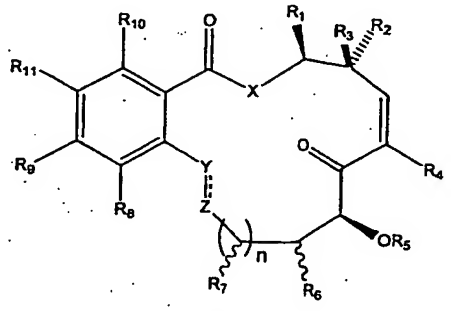
118. The method of claim 84, comprising administering a compound having the structure:



or pharmaceutically acceptable salt, ester, or salt of ester thereof.

119. A method for providing protection against UVB-induced photodamage to a subject, said method comprising:

Administering to the subject in need thereof a composition comprising a compound having the structure:



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or pharmaceutically acceptable salt, ester, or salt of ester thereof;

wherein R_1 is hydrogen, straight or branched C_{1-6}alkyl, straight or branched C_{1-6}heteroalkyl, or aryl,

wherein the alkyl, heteroalkyl, and aryl groups may optionally be substituted with one or more occurrences of halogen, hydroxyl or protected hydroxyl;

R_2 and R_3 are each independently hydrogen, halogen, hydroxyl, protected hydroxyl, straight or branched C_{1-6}alkyl, straight or branched C_{1-6}heteroalkyl, or aryl,

wherein the alkyl, heteroalkyl, and aryl groups may optionally be substituted with one or more occurrences of halogen, hydroxyl or protected hydroxyl; or

R_1 and R_2, when taken together, may form a saturated or unsaturated cyclic ring of 3 to 8 carbon atoms, optionally substituted with one or more occurrences of halogen; or

R_1 and R_3, when taken together, may form a saturated or unsaturated cyclic ring of 3 to 8 carbon atoms, optionally substituted with one or more occurrences of halogen;

R_4 is hydrogen or halogen;

R_5 is hydrogen or a protecting group;

R_6 is hydrogen, hydroxyl, or protected hydroxyl;

n is 0-2;

R_7, for each occurrence, is independently hydrogen, hydroxyl, or protected hydroxyl;

R_8 is hydrogen, halogen, hydroxyl, protected hydroxyl, alkyloxy, or C_{1-6}alkyl optionally substituted with hydroxyl, protected hydroxyl, SR_{12}, or $NR_{12}R_{13}$;

R_9 is hydrogen, halogen, hydroxyl, protected hydroxyl, OR_{12}, SR_{12}, $NR_{12}R_{13}$, $-X_1(CH_2)_pX_2-R_{14}$, or is C_{1-6}alkyl optionally substituted with hydroxyl, protected hydroxyl, halogen, amino, protected amino, or $-X_1(CH_2)_pX_2-R_{14}$;

wherein R_{12} and R_{13} are, independently for each occurrence, hydrogen, C_{1-6}alkyl, aryl, heteroaryl, alkylaryl, or alkylheteroaryl, or a protecting group, or R_{12} and R_{13}, taken together may form a saturated or unsaturated cyclic ring containing 1 to 4 carbon atoms and 1 to 3 nitrogen or oxygen atoms, and each of R_{12} and R_{13} are optionally further substituted with one or more occurrences of hydroxyl, protected hydroxyl, alkyloxy, amino, protected amino, alkylamino, aminoalkyl, or halogen,

wherein X_1 and X_2 are each independently absent, or are oxygen, NH, or -N(alkyl), or wherein X_2-R_{14} together are N_3 or are a saturated or unsaturated heterocyclic moiety,

p is 2-10, and

R_{14} is hydrogen, or an aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, or is $-(C=O)NHR_{15}$ $-(C=O)OR_{15}$, or $-(C=O)R_{15}$, wherein each

occurrence of R_{15} is independently hydrogen, alkyl, heteroalkyl, aryl, heteroaryl, alkylaryl, or alkylheteroaryl, or R_{14} is $-SO_2(R_{16})$, wherein R_{16} is an alkyl moiety, wherein one or more of R_{14}, R_{15}, or R_{16} are optionally substituted with one or more occurrences of hydroxyl, protected hydroxyl, alkyloxy, amino, protected amino, alkylamino, aminoalkyl, or halogen; or

R_8 and R_9 may, when taken together, form a saturated or unsaturated cyclic ring containing 1 to 4 carbon atoms and 1 to 3 nitrogen or oxygen atoms and is optionally substituted with hydroxyl, protected hydroxyl, alkyloxy, amino, protected amino, alkylamino, aminoalkyl, or halogen;

R_{10} is hydrogen, hydroxyl, protected hydroxyl, amino, or protected amino;

R_{11} is hydrogen, hydroxyl or protected hydroxyl;

X is absent or is O, NH, N-alkyl, CH_2 or S;

Y is CHR_{17}, O, C=O, CR_{17} or NR_{17}; and Z is CHR_{18}, O, C=O, CR_{18} or NR_{18}, wherein each occurrence of R_{17} and R_{18} is independently hydrogen or C_{1-6}alkyl, or R_{17} and R_{18} taken together is –O-, $-CH_2-$ or $-NR_{19}-$, wherein R_{19} is hydrogen or C_{1-6}alkyl, and Y and Z may be connected by a single or double bond; and

a pharmaceutically acceptable carrier or diluent.

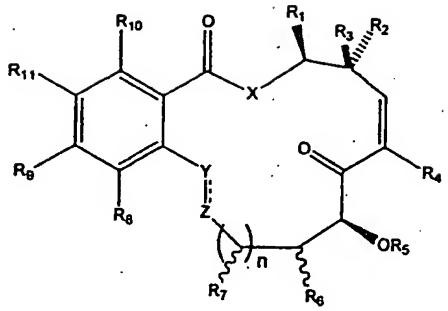
120. The method of claim 119, wherein in the step of administering, the composition is administered topically.

121. The method of claim 119, wherein the photodamage is skin wrinkles.

122. The method of claim 119, wherein the photodamage is a skin cancer.

123. A method for preventing or reducing the rate of restenosis, comprising:

inserting a stent into an obstructed blood vessel, the stent having a generally tubular structure, the surface of the structure being coated with (or otherwise adapted to release) a composition comprising a compound having the structure:



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or pharmaceutically acceptable salt, ester, or salt of ester thereof;

wherein R_1 is hydrogen, straight or branched C_{1-6}alkyl, straight or branched C_{1-6}heteroalkyl, or aryl,

wherein the alkyl, heteroalkyl, and aryl groups may optionally be substituted with one or more occurrences of halogen, hydroxyl or protected hydroxyl;

R_2 and R_3 are each independently hydrogen, halogen, hydroxyl, protected hydroxyl, straight or branched C_{1-6}alkyl, straight or branched C_{1-6}heteroalkyl, or aryl,

wherein the alkyl, heteroalkyl, and aryl groups may optionally be substituted with one or more occurrences of halogen, hydroxyl or protected hydroxyl; or

R_1 and R_2, when taken together, may form a saturated or unsaturated cyclic ring of 3 to 8 carbon atoms, optionally substituted with one or more occurrences of halogen; or

R_1 and R_3, when taken together, may form a saturated or unsaturated cyclic ring of 3 to 8 carbon atoms, optionally substituted with one or more occurrences of halogen;

R_4 is hydrogen or halogen;

R_5 is hydrogen or a protecting group;

R_6 is hydrogen, hydroxyl, or protected hydroxyl;

n is 0-2;

R_7, for each occurrence, is independently hydrogen, hydroxyl, or protected hydroxyl;

R_8 is hydrogen, halogen, hydroxyl, protected hydroxyl, alkyloxy, or C_{1-6}alkyl optionally substituted with hydroxyl, protected hydroxyl, SR_{12}, or $NR_{12}R_{13}$;

R_9 is hydrogen, halogen, hydroxyl, protected hydroxyl, OR_{12}, SR_{12}, $NR_{12}R_{13}$, $-X_1(CH_2)_pX_2-R_{14}$, or is C_{1-6}alkyl optionally substituted with hydroxyl, protected hydroxyl, halogen, amino, protected amino, or $-X_1(CH_2)_pX_2-R_{14}$;

wherein R_{12} and R_{13} are, independently for each occurrence, hydrogen, C_{1-6}alkyl, aryl, heteroaryl, alkylaryl, or alkylheteroaryl, or a protecting group, or R_{12} and R_{13}, taken together may form a saturated or unsaturated cyclic ring containing 1 to 4 carbon atoms and 1 to 3 nitrogen or oxygen atoms, and each of R_{12} and R_{13} are optionally further substituted with one or more occurrences of hydroxyl, protected hydroxyl, alkyloxy, amino, protected amino, alkylamino, aminoalkyl, or halogen,

wherein X_1 and X_2 are each independently absent, or are oxygen, NH, or -N(alkyl), or wherein X_2-R_{14} together are N_3 or are a saturated or unsaturated heterocyclic moiety,

p is 2-10, and

R_{14} is hydrogen, or an aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, or is $-(C=O)NHR_{15}$ $-(C=O)OR_{15}$, or $-(C=O)R_{15}$, wherein each occurrence of R_{15} is independently hydrogen, alkyl, heteroalkyl, aryl, heteroaryl, alkylaryl, or alkylheteroaryl, or R_{14} is $-SO_2(R_{16})$, wherein R_{16} is an alkyl moiety, wherein one or more of R_{14}, R_{15}, or R_{16} are optionally substituted with one or more occurrences of hydroxyl, protected hydroxyl, alkyloxy, amino, protected amino, alkylamino, aminoalkyl, or halogen; or

R_8 and R_9 may, when taken together, form a saturated or unsaturated cyclic ring containing 1 to 4 carbon atoms and 1 to 3 nitrogen or oxygen atoms and is optionally substituted with hydroxyl, protected hydroxyl, alkyloxy, amino, protected amino, alkylamino, aminoalkyl, or halogen;

R_{10} is hydrogen, hydroxyl, protected hydroxyl, amino, or protected amino;

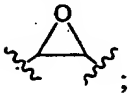
R_{11} is hydrogen, hydroxyl or protected hydroxyl;

X is absent or is O, NH, N-alkyl, CH_2 or S;

Y is CHR_{17}, O, C=O, CR_{17} or NR_{17}; and Z is CHR_{18}, O, C=O, CR_{18} or NR_{18}, wherein each occurrence of R_{17} and R_{18} is independently hydrogen or C_{1-6}alkyl, or R_{17} and R_{18} taken together is –O-, $-CH_2-$ or $-NR_{19}-$, wherein R_{19} is hydrogen or C_{1-6}alkyl, and Y and Z may be connected by a single or double bond; and optionally

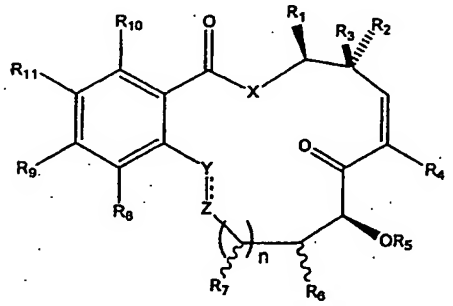
a pharmaceutically acceptable carrier or diluent;

such that the obstruction is eliminated and the composition is delivered in amounts effective to prevent or reduce the rate of restenosis;

with the proviso that the following groups do not occur simultaneously as defined: n is 1; X is O; R_1 is methyl; R_2, R_3, R_4, R_7, R_8 and R_{11} are each hydrogen; R_5 is hydrogen, C_{1-4}alkyl or $-C(=O)C_{1-4}$alkyl; R_6 is hydrogen, OH, C_{1-4}alkoxy or $-OC(=O)C_{1-4}$alkyl; R_9 and R_{10} are independently OH, C_{1-4}alkoxy or $-OC(=O)C_{1-4}$alkyl; and Y-Z is $-CHR^YCHR^Z-$, $-CH=CH-$ or  ; wherein R^Y and R^Z are independently hydrogen, C_{1-4}alkyl or C_{1-4}alkanoyl.

124. A method for expanding the lumen of a body passageway, comprising:

inserting a stent into the passageway, the stent having a generally tubular structure, the surface of the structure being coated with (or otherwise adapted to release) a composition comprising a compound having the structure:



(I)

or pharmaceutically acceptable salt, ester, or salt of ester thereof;

wherein R_1 is hydrogen, straight or branched C_{1-6}alkyl, straight or branched C_{1-6}heteroallkyl, or aryl,

wherein the alkyl, heteroalkyl, and aryl groups may optionally be substituted with one or more occurrences of halogen, hydroxyl or protected hydroxyl;

R_2 and R_3 are each independently hydrogen, halogen, hydroxyl, protected hydroxyl, straight or branched C_{1-6}alkyl, straight or branched C_{1-6}heteroalkyl, or aryl,

wherein the alkyl, heteroalkyl, and aryl groups may optionally be substituted with one or more occurrences of halogen, hydroxyl or protected hydroxyl; or

R_1 and R_2, when taken together, may form a saturated or unsaturated cyclic ring of 3 to 8 carbon atoms, optionally substituted with one or more occurrences of halogen; or

R_1 and R_3, when taken together, may form a saturated or unsaturated cyclic ring of 3 to 8 carbon atoms, optionally substituted with one or more occurrences of halogen;

R_4 is hydrogen or halogen;

R_5 is hydrogen or a protecting group;

R_6 is hydrogen, hydroxyl, or protected hydroxyl;

n is 0-2;

R_7, for each occurrence, is independently hydrogen, hydroxyl, or protected hydroxyl;

R_8 is hydrogen, halogen, hydroxyl, protected hydroxyl, alkyloxy, or C_{1-6}alkyl optionally substituted with hydroxyl, protected hydroxyl, SR_{12}, or $NR_{12}R_{13}$;

R_9 is hydrogen, halogen, hydroxyl, protected hydroxyl, OR_{12}, SR_{12}, $NR_{12}R_{13}$, $-X_1(CH_2)_pX_2-R_{14}$, or is C_{1-6}alkyl optionally substituted with hydroxyl, protected hydroxyl, halogen, amino, protected amino, or $-X_1(CH_2)_pX_2-R_{14}$;

wherein R_{12} and R_{13} are, independently for each occurrence, hydrogen, C_{1-6}alkyl, aryl, heteroaryl, alkylaryl, or alkylheteroaryl, or a protecting group, or R_{12} and R_{13}, taken together may form a saturated or unsaturated cyclic ring containing 1 to 4 carbon atoms and 1 to 3 nitrogen or oxygen atoms, and each of R_{12} and R_{13} are optionally further substituted with one or more occurrences of hydroxyl, protected hydroxyl, alkyloxy, amino, protected amino, alkylamino, aminoalkyl, or halogen,

wherein X_1 and X_2 are each independently absent, or are oxygen, NH, or -N(alkyl), or wherein X_2-R_{14} together are N_3 or are a saturated or unsaturated heterocyclic moiety,

p is 2-10, and

R_{14} is hydrogen, or an aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, or is $-(C=O)NHR_{15}$ $-(C=O)OR_{15}$, or $-(C=O)R_{15}$, wherein each

occurrence of R_{15} is independently hydrogen, alkyl, heteroalkyl, aryl, heteroaryl, alkylaryl, or alkylheteroaryl, or R_{14} is $-SO_2(R_{16})$, wherein R_{16} is an alkyl moiety, wherein one or more of R_{14}, R_{15}, or R_{16} are optionally substituted with one or more occurrences of hydroxyl, protected hydroxyl, alkyloxy, amino, protected amino, alkylamino, aminoalkyl, or halogen; or

R_8 and R_9 may, when taken together, form a saturated or unsaturated cyclic ring containing 1 to 4 carbon atoms and 1 to 3 nitrogen or oxygen atoms and is optionally substituted with hydroxyl, protected hydroxyl, alkyloxy, amino, protected amino, alkylamino, aminoalkyl, or halogen;

R_{10} is hydrogen, hydroxyl, protected hydroxyl, amino, or protected amino;

R_{11} is hydrogen, hydroxyl or protected hydroxyl;

X is absent or is O, NH, N-alkyl, CH_2 or S;

Y is CHR_{17}, O, C=O, CR_{17} or NR_{17}; and Z is CHR_{18}, O, C=O, CR_{18} or NR_{18}, wherein each occurrence of R_{17} and R_{18} is independently hydrogen or C_{1-6}alkyl, or R_{17} and R_{18} taken together is –O-, $-CH_2-$ or $-NR_{19}-$, wherein R_{19} is hydrogen or C_{1-6}alkyl, and Y and Z may be connected by a single or double bond; and optionally

a pharmaceutically acceptable carrier or diluent;

such that the passageway is expanded.

125. The method of claim 124, wherein the lumen of a body passageway is expanded in order to eliminate a biliary, gastrointestinal, esophageal, tracheal/bronchial, urethral and/or vascular obstruction.

126. The method of claim 125, wherein the lumen of a body passageway is expanded in order to eliminate a vascular obstruction.